

## **REMARKS**

Applicants respectfully request reconsideration of the following arguments.

### **1. Status of the Claims**

Claims 1-8 and 10 stand pending. Claim 10 stands withdrawn. Claims 1-8 stand rejected. Claim 9 stands previously canceled.

The Office is respectfully reminded that the withdrawn claim 10 is eligible for rejoinder once the composition claims are found allowable. Because the present claims are allowable, rejoinder of claim 10 and examination on the merits of the same is requested in the next communication from the Office.

### **2. Acknowledgement of Information Disclosure Statements**

Applicants appreciate the Office's acknowledgement of the Information Disclosure Statement filed October 21, 2009.

### **3. Withdrawn Objections and Rejections**

Applicants appreciate the Office's withdrawal of the following objections and rejections:

- 1) the objection to the Specification for allegedly containing two Abstracts;
- 2) the objection to the Specification for allegedly non-conforming use of trademarks;
- 3) the indefiniteness rejection of claims 6-9; and
- 4) the obviousness rejection of claims 1-9 over **Hara** et al. (JP 05-013647) in view of **Maeda** et al. (WO03/057707) in light of **Takeda** et al. (U.S. Published Application No. 2002/0031574).

Office Action, pages 2-3.

### **4. Rejection of the Claims Under 35 U.S.C. § 103(a)**

The Office newly rejects claims 1-8 under 35 U.S.C. § 103(a) as allegedly unpatentable over **Ito** et al., JP 05013647 ("Ito") in view of **Shimono** et al., JP06263790 A ("Shimono"). Ito

allegedly discloses a vitamin C rich fruit juice drink comprising fruit juice, kojic acid, and ascorbic acid. *Id.*, at 5. The Office admits that Ito does not disclose the claimed 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid. *Id.*, at 6. The Office, however, interprets the claimed "process koji" to include "any crude extract or isolated compound from koji (koji mold)." *Id.*, at 5-6. The Office then asserts that the claimed "processed koji" reads upon the kojic acid of Ito, because kojic acid is allegedly derived from koji mold. *Id.* Shimono, the secondary reference, is relied upon for allegedly disclosing 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid and its various desirable properties. *Id.*, at 6. The Office concludes that it would have been obvious to substitute the ascorbic acid for the provitamin C compound 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid to reach the claimed composition. *Id.*, at 6-7.

Applicants traverse. To render a claim obvious, both the suggestion of the claimed invention and the expectation of success must be in the prior art, not from the disclosure of the claimed invention. *In re Dow Chem. Co.*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). Additionally, "obviousness requires a suggestion of *all* limitations in a claim." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1342, 68 U.S.P.Q.2d 1940, 1947 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985, 180 U.S.P.Q. 580, 583 (C.C.P.A. 1974) (emphasis added)). Furthermore, one ordinarily skilled in the art would have had a reasonable expectation of success to practice the claimed invention. *Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc.*, 72 Fed. Reg. 57,528.

The Office fails to adduce *prima facie* obviousness, because the cited references fail to teach or suggest all claim elements. Claims 1-9 recite, at least, a composition comprising (1) 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid, and (2) a koji mold or a processed koji. The Office admits that Ito does not disclose 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid. Shimono is relied upon for its purported teaching of 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid and its desirable properties. The Office is respectfully reminded that Shimono in fact discloses 2-O- $\beta$ -D-galactopyranosyl-L-ascorbic acid, which is *not* 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid. 2-O- $\beta$ -D-galactopyranosyl-L-ascorbic acid has a different carbohydrate moiety from 2-O-( $\beta$ -D-

glucopyranosyl)ascorbic acid.<sup>1</sup>  $\beta$ -D-glucopyranose, the carbohydrate moiety of claimed 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid, is different from  $\beta$ -D-galactopyranose, which is the carbohydrate moiety of 2-O- $\beta$ -D-galactopyranosyl-L-ascorbic acid. Additional to structural difference, the two carbohydrate moieties have distinct physicochemical properties, *e.g.*, melting point and specific rotation ( $[\alpha]_D$ ). The Office is directed to the following table:

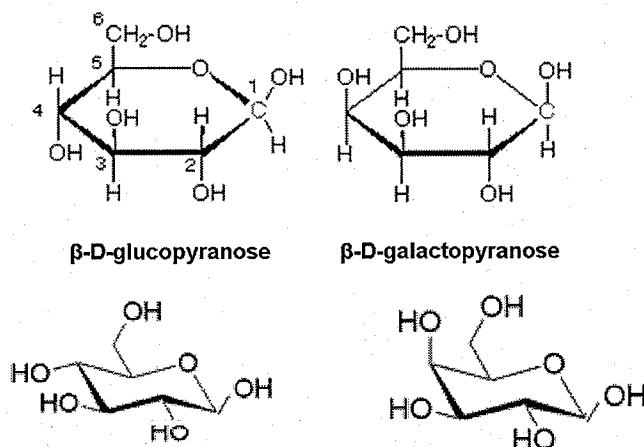
	$\beta$ -D-glucopyranose	$\beta$ -D-galactopyranose
<b>Melting Point</b>	148-155°C	167°C
<b><math>[\alpha]_D</math></b>	+18.7	+52.8

See The Merck Index, 13<sup>th</sup> Ed., 2001, pages 770 and 794 (enclosed as **Appendix I**).

In view of the above arguments, Shimono does not teach claimed 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid. Accordingly, Shimono cannot cure Ito's defect. Ito and Shimono, alone or viewed in combination, fail to teach or suggest the claimed 2-O-( $\beta$ -D-glucopyranosyl)ascorbic acid.

Furthermore, neither reference teaches or suggests the claimed koji mold or processed koji. The Office's interpretation of the term "processed koji" is unsupported. Although the Office may give a claim term its broadest reasonable interpretation during prosecution, "claim language should be read in light of the specification as it would be interpreted by one of ordinary

<sup>1</sup> The two carbohydrate moieties differ at the position 4 of the 6-membered sugar ring as shown below:



skill in the art.” *In re Am. Acad. Of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364, 70 U.S.P.Q.2d 1827, 1830 (Fed. Cir. 2004) (citing *In re Bond*, 910 F.2d 831, 833, 15 U.S.P.Q.2d 1566 (Fed. Cir. 1990)). Applicants direct the Office to the page 18, lines 3-12 of the Substitute Specification:

A processed koji can be used **as far as an enzyme contained in the koji mold is not inactivated.** A processed koji may be, for example, a dried koji mold. ... Further, a processed koji may be an extract of a koji mold. An extract may be an extract of cells obtained by treating koji mold cells using the means known per se such as immersion, grinding and the like.

(emphasis added). In light of the Specification, a skilled artisan would understand that the claimed “processed koji” must contain active koji enzyme(s). The Office apparently ignores such a limitation. Accordingly, a skilled artisan would not have interpreted the “processed koji” only be kojic acid, which fails to contain any active koji enzyme. Shimono does not teach or suggest the claimed koji mold or processed koji either. Ito and Shimono, alone or viewed in combination, fails to teach or suggest the claimed koji mold or processed koji.

The cited references fail to teach or suggest at least the above-discussed claim elements. Without all claim elements taught, there can be no expectation to make and/or use the claimed composition. Claims 1-8 are thus non-obvious over cited art. Applicants respectfully request withdrawal of the rejection and allowance of the claims.

### CONCLUSION

Should the Office have any questions or comments regarding Applicants' amendments or response, please contact Applicants' undersigned representative at (202) 842-8821.

Furthermore, please direct all correspondence to the below-listed address.

In the event that the Office believes that there are fees outstanding in the above-referenced matter and for purposes of maintaining pendency of the application, the Office is authorized to charge the outstanding fees to Deposit Account No. 50-0573. The Office is likewise authorized to credit any overpayment to the same Deposit Account Number.

Respectfully Submitted,

Date: January 28, 2010

By: Brian Lathrop Reg. No. 43,740  
for Mercedes K. Meyer, Ph.D., Esq.  
Registration No. 44,939

DRINKER BIDDLE & REATH LLP

Customer No. **55694**

1500 K Street, N.W., Suite 1100

Washington, D.C. 20005-1209

Tel. No.: (202) 842-8800

Fax No.: (202) 842-8465

# Appendix I

# THE MERCK INDEX

AN ENCYCLOPEDIA OF  
CHEMICALS, DRUGS, AND BIOLOGICALS

THIRTEENTH EDITION

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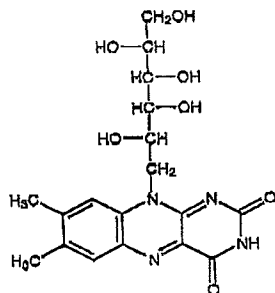
## Galactoflavin

Crystals from methanol + water, mp 188-189°. Slightly sweet taste.  $d_{20}^{25}$  1.47. bp, 275-280°. One gram dissolves in 30 ml water, in 2 ml boiling water. Slightly sol in alc.  $K_a$  at 18° =  $3.5 \times 10^{-14}$ .

Hexa-*O*-acetyl-galactitol.  $C_{18}H_{26}O_{12}$ . Crystals from ethanol, mp 168-169°.

Hexanitrate. Nitrodulcitol. mp 94-95°. Has explosive properties: Taylor, Rinkenbach, *J. Franklin Inst.* 204, 374 (1927).

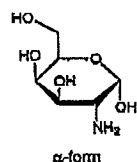
4354. Galactoflavin. [5735-19-3] 1-Deoxy-1-(3,4-dihydro-7,8-dimethyl-2,4-dioxobenzo[*g*]pteridin-10(2*H*)-yl)-D-galactitol; 7,8-dimethyl-10-(D-galacto-2,3,4,5,6-pentahydroxyhexyl)benzo[*g*]pteridine-2,4(3*H*,10*H*)-dione; 7,8-dimethyl-10-(D-galacto-2,3,4,5,6-pentahydroxyhexyl)isoalloxazine; 7,8-dimethyl-10-(*d*-1'-dulcetyl)isoalloxazine; 6,7-dimethyl-9-(*d*-1'-dulcetyl)isoalloxazine; 6,7-dimethyl-9-(1-deoxy-D-galactitol-1-yl)isoalloxazine.  $C_{18}H_{22}N_4O_7$ ; mol wt 406.39. C 53.20%, H 5.46%, N 13.79%, O 27.56%. Prep'd from 1-deoxy-1-(3,4-dimethyl-6-phenylazo)anilino-D-galactitol and barbituric acid: Borzovskii, Eremenko, *Zh. Obshch. Khim.* 32, 4056 (1962), C.A. 59, 736b (1963). Structure: Emerson *et al.*, *J. Biol. Chem.* 160, 165 (1945). Pharmacology: Lane, Brindley, *Proc. Soc. Exp. Biol. Med.* 116, 57 (1964). Produces congenital malformations in animals: Nelson *et al.*, *J. Nutr.* 58, 125 (1956); Miller *et al.*, *J. Biol. Chem.* 237, 968 (1962); Mackler, *Pediatrics* 43, 915 (1969).



Yellow crystals, dec 260°. Absorption max: 223, 267, 370, 445 nm ( $\epsilon$  2730, 28100, 9100, 10800). Compd has yellow-green fluorescence in water.

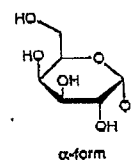
USE: Riboflavine antagonist.

4355. D-Galactosamine. [7535-00-4] 2-Amino-2-deoxy-D-galactose; chondrosamine; GalN.  $C_6H_{13}NO_5$ ; mol wt 179.17. C 40.22%, H 7.31%, N 7.82%, O 44.65%. Amino sugar isolated from chondroitin sulfate, q.v.: P. A. Levene, F. B. La Forge, *J. Biol. Chem.* 18, 123 (1914). Sep'n of  $\alpha$ - and  $\beta$ -anomers: P. A. Levene, *ibid.* 57, 337 (1923). Synthesis: S. P. James *et al.*, *Nature* 156, 308 (1945) *idem.*, *J. Chem. Soc.* 1946, 625; R. Kuhn, W. Kirschenlohr, *Ann.* 600, 126 (1956); P. A. Gent *et al.*, *J. Chem. Soc. Perkin Trans. 1* 1972, 277. Chemistry: D. Horton in *The Amino Sugars* Vol. 1A, R. W. Jeanloz, Ed. (Academic, New York, 1969) pp 133-145. Inducer of exptl hepatitis: D. Keppler *et al.*, *Exp. Mol. Pathol.* 9, 279 (1968); K. Decker, D. Keppler in *Progress in Liver Diseases* Vol. IV, H. Popper, F. Schaffner, Eds. (Grune & Stratton, New York, 1972) p 183. Powerful inhibitor of hepatic RNA synthesis: D. Keppler *et al.*, *J. Biol. Chem.* 249, 211 (1974); T. Anukarahanonta *et al.*, *Eur. J. Cancer* 16, 1171 (1980).

 $\alpha$ -form

Hydrochloride.  $C_6H_{14}ClNO_5$ . Crystals, mp 180° (dec). Shows mutarotation.  $\alpha$ -Form:  $[\alpha]_D^{25} +124^\circ \rightarrow +93^\circ$  (water).  $\beta$ -Form:  $[\alpha]_D^{25} +47^\circ \rightarrow +93^\circ$  (water).

4356. D-Galactose. [59-23-4] Cerebrose; brain sugar.  $C_6H_{12}O_6$ ; mol wt 180.16. C 40.00%, H 6.71%, O 53.28%. Constituent of many oligo- and polysaccharides occurring in pectins, gums, and mucilages. Prepn: Kent, Tollens, *Ann.* 227, 224 (1885); E. P. Clark, *J. Biol. Chem.* 47, 2 (1921). Mutarotation and purification of  $\beta$ -form: C. S. Hudson, E. Yanosky, *J. Am. Chem. Soc.* 39, 1021 (1917). Structural configuration: J. Pryde, *J. Chem. Soc.* 123, 1809 (1923); W. Charlton *et al.*, *ibid.* 1926, 94; W. N. Haworth *et al.*, *ibid.* 1927, 2428; E. L. Jackson, C. S. Hudson, *J. Am. Chem. Soc.* 59, 994 (1937); R. M. Hann *et al.*, *ibid.* 66, 1912 (1944). Isolin in the processing of the red algae, *Porphyra umbilicalis*: S. Peat *et al.*, *J. Chem. Soc.* 1961, 1590. Review: W. Pigman, *The Carbohydrates* (Academic Press, New York, 1957) pp 88-90. Review of diagnostic use: W. J. Schirmer *et al.*, *J. Surg. Res.* 41, 543 (1986).

 $\alpha$ -form

$\alpha$ -Form. Prisms from water or ethanol, mp 167°.  $[\alpha]_D^{25} +150.7^\circ \rightarrow +80.2^\circ$  (water). Soluble in about 0.5 parts water, freely sol in hot water; final soln in water at 25° = 68%; sol in pyridine; slightly sol in alcohol.

$\beta$ -Form. Crystals, mp 167°.  $[\alpha]_D^{25} +52.8^\circ \rightarrow +80.2^\circ$  (water). Sol in 1.7 parts water at 17°.

Monohydrate. Prisms from water, mp 118-120°.

Microparticulate form. [90881-70-2] SH U 454; Echovist. Suspension of galactose microparticle granules in a galactose solution. Prepn: J. S. Rasor, E. G. Tickner, EP 131540 (1986 to Schering). Series of articles on *in vivo* use in echocardiography: *Arzneimittel-Forsch.* 36, 1030-1040 (1986). Review of formulations and clinical diagnostic use: R. Schürmann, R. Schliel, *Radio. Med.* 87, Suppl. 1, 15-23 (1994).

Transpulmonary microparticulate form. [144046-30-0] SH U 508A; Levovist. Suspension of galactose microparticle granules containing 0.1% physiologic palmitic acid in a sterile water solution.

THERAP CAT: Diagnostic aid (hepatic function). Microparticulate forms as diagnostic aid (ultrasound contrast agent).

4357.  $\alpha$ -Galactosidase A. Ceramide trihexosidase. Lysosomal enzyme that hydrolyzes terminal  $\alpha$ -D-galactose residues in oligosaccharides and galactolipids. Genetic deficiency of the enzyme results in the glycosphingolipid storage disorder known as Fabry's disease. Homodimeric glycoprotein, mol wt ~101 kDa. Targeted to lysosomes via the mannose-6-phosphate receptor. Identification and role in disease: R. O. Brady *et al.*, *N. Engl. J. Med.* 276, 1163 (1967). Identification as  $\alpha$ -galactosidase: J. A. Kint, *Science* 167, 1268 (1970). Use in enzyme replacement therapy: R. J. Desnick *et al.*, *Proc. Nat. Acad. Sci. USA* 76, 5326 (1979). Review: R. J. Desnick *et al.*, in *The Metabolic and Molecular Bases of Inherited Disease*, C. R. Scriver *et al.*, Eds. (McGraw-Hill, New York, 7th Ed., 1995) pp 2741-2784.

Agalsidase alfa. Replagal. Human  $\alpha$ -galactosidase A produced by recombinant DNA technology in cultured human cells. See: R. F. Selden *et al.*, WO 98 11206 (1998 to Transkaryotic Therapies). Clinical pharmacology and pharmacokinetics: R. Schiffmann *et al.*, *Proc. Nat. Acad. Sci. USA* 97, 365 (2000). Agalsidase beta. Fabrazyme. Human  $\alpha$ -galactosidase A produced by recombinant DNA technology in Chinese hamster ovary cells. See: R. J. Desnick *et al.*, US 5356804 (1994 to Mount Sinai School of Med.).

THERAP CAT: E case.

4358. D-Gale 194.14. C 37.12% ysis of pectin whei lich, *Chem. Ztg.* 4 Z 259, 100 (1933) *Chem.* 95, 203 (1935 (1933); Ande from mustard seed prod.).

$\alpha$ -Form. Mon +50.9° (water). Practically insol in  $\beta$ -Form. mp 1 Phenylhydrazo

4359. Galan nese ginger. Drie giberaceae. Habi frid, galangin, di

4360. Galan 4H-1-benzopyrun  $C_{15}H_{10}O_2$ ; mol w Isolin from galang acerization: E. J R. Robinson, J. C Robinson, *ibid.* 1 Grogor, L. Jurd, 1 Dietrich, *ibid.* 66,

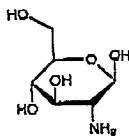
Yellowish nece sol in ethanol, et benzene.

4361. Galat 5,9,10,11,12-Hex [3a,3,2-*a'*][2]ben nyl:  $C_{17}H_{21}NO_2$ ; O 16.70%. Seice Caucasian anowd Gezer, N. P. Pros 1899 (1952); fror (1957). Structur (London) 1956, 1 Burton, G. W. X *Chem. Soc.* 1962 Dityrosine: K. St synthesis studies 4543; W. Dobk andy: S. L. Fri (1961). Clinical *macol. Ther.* 50, Harvey, Pharma



## 4472

Setnikar *et al.*, *Arzneimittel-Forsch.* 36, 729 (1986). Clinical trials in arthrosis: Y. Vajarudal, *Clin. Ther.* 3, 336 (1981); M. J. Tapadinhas *et al.*, *Pharmatherapeutica* 3, 157 (1982). Review: Foster, Stacey, "The Chemistry of the 2-Amino Sugars" in C. S. Hudson *et al.*, *Advan. Carbohydr. Chem.* vol. 7 (Academic Press, New York, 1952) pp 247-288.



$\alpha$ -Form. [28905-11-5] Crystals, mp 88°.  $[\alpha]_D^{20} +100^\circ$  changing to  $+47.5^\circ$  after 30 min (water).

$\beta$ -Form. [28905-10-4] Needles from methanol, dec 110°.  $[\alpha]_D^{20} +28^\circ$  changing to  $+47.5^\circ$  after 30 min (water). Very sol in water, sol in about 38 parts boiling methanol; sparingly sol in cold methanol or ethanol. Practically insol in ether, chloroform.

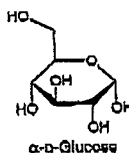
N-Acetylglucosamine. [7512-17-6]  $C_8H_{13}NO_6$ . Needles from methanol + ether, mp 205°.  $[\alpha]_D^{20} +64^\circ$  changing to  $+40.9^\circ$  (in water).

Sulfate salt. [29031-19-4] Dona.  $C_8H_{13}NO_6 \cdot xH_2SO_4$ .

USE: Pharmaceutical aid.

THERAP CAT: Antiarthritic.

→ 4472. Glucose. [50-99-7] D-Glucose; dextrose; blood sugar; grape sugar; corn sugar; Dextropur; Dextrosol; Glucolin.  $C_6H_{12}O_6$ ; mol wt 180.16. C 40.00%, H 6.71%, O 53.28%. A main source of energy for living organisms. Occurs naturally and in the free state in fruits and other parts of plants. Combined in glucosides, in di- and oligosaccharides, in the polysaccharides cellulose and starch, and in glycogen. Normal human blood contains 0.08-0.1%. Manuf on a large scale from starch: Denn, Gottfried, *Advan. Carbohydr. Chem.* 5, 127 (1950). Below 50°,  $\alpha$ -D-glucose hydrate is the stable cryst form, above 50° the anhyd form is obtained and at still higher temps  $\beta$ -D-glucose is formed: W. Pigman, *The Carbohydrates* (Academic Press, New York, 1957) p 92. Structure: Kjaer, Lindberg, *Acta Chem. Scand.* 13, 1713 (1959). Conformation: E. Percival, *Structural Carbohydrate Chemistry* (J. Garnet Miller, London, 1962) pp 51-57. Comprehensive monograph: H. Bartelheimer *et al.*, *D-Glucose und verwandte Verbindungen in Medizin und Biologie* (Bake, Stuttgart, 1966) 1126 pp.



$\alpha$ -Form monohydrate. Crystals from water, mp 83°.  $[\alpha]_D^{20} +102.0^\circ \rightarrow +47.9^\circ$  (water). 0.74 times as sweet as sucrose. One gram dissolves in about 1 ml water and in about 60 ml alcohol.

$\alpha$ -Form anhydr. Crystals from hot ethanol or water, mp 146°.  $[\alpha]_D^{20} +112.2^\circ \rightarrow +52.7^\circ$  (c = 10 in water). The final value is obtained instantly in the presence of hydroxyl ions. Formula for varying concns:  $[\alpha]_D^{20} +52.5^\circ + 0.0188p$  (p = g/100 ml). pH of 0.5 molar aq soln 5.9.  $d_4^{20}$  of water solns w/v: 5% = 1.019; 10% = 1.038; 20% = 1.076; 30% = 1.113; 40% = 1.149.  $n_D^{20}$  10% soln 1.3479. One gram dissolves in 1.1 ml water at 25°; in 0.8 ml at 30°; in 0.41 ml at 50°; in 0.28 ml at 70°; in 0.18 ml at 90°; in 120 ml methanol at 20°. Very sparingly sol in abs alcohol, ether, acetone; sol in hot glacial acetic acid, pyridine, aniline.

→  $\beta$ -Form. Crystals from hot water + ethanol, from dil acetic acid, or from pyridine, mp 148-155°.  $[\alpha]_D^{20} +18.7^\circ \rightarrow +52.7^\circ$  (c = 10 in water).

## Glucose

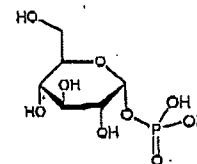
THERAP CAT: Fluid and nutrient replenisher.  
THERAP CAT (VET): Nutridon (usually parenterally), hypoglycemia, ketosis, to counteract hepatotoxins.

4473. Glucose Oxidase. [9001-37-0]  $\beta$ -D-Glucopyranose aerodehydrogenase; P-FAD; corylophylase; microcide; mikrosid; notatin. An enzyme obtained from mycelia of fungi, such as *Aspergillus* and *Penicillium*; a typical aerobic dehydrogenase which catalyzes the oxidation of glucose to gluconic acid (molecular oxygen is reduced to hydrogen peroxide). It is a flavoprotein, the prosthetic group being flavine-adenine dinucleotide (FAD). Commercial preps frequently contain appreciable amounts of another enzyme, catalase, which is desirable for certain uses since it removes hydrogen peroxide aerobically generated by glucose oxidase. Names of some commercial preps are: *DesO*, *Fermeazyme*, *OxyBan*, *Ovazyme*. Isola from *Penicillium* cultures: Coulthard *et al.*, *Biochem. J.* 39, 24 (1945). Commercial production from *Aspergillus* and *Penicillium*: Goldsmith *et al.*, US 2926122 (1960); from *Aspergillus niger*: Farnsworth *et al.*, US 3102081 (1963 to Miles Labs.). Removal of proteolytic enzymes from glucose oxidase (contg catalase) obtained from *Aspergillus* or *Penicillium* cultures: Ohlmeyer, US 2940904 (1960 to Ben L. Saret). Separation from catalase: Pazur *et al.*, *Biochem. Biophys. Acta* 65, 369 (1962). Properties: Muller, *Enzymologia* 10, 40 (1941); Kellin, Harter, *Biochem. J.* 42, 221 (1948), 50, 331 (1952). Reviews: L. A. Underkofler "Glucose Oxidase: Production, Properties, Present and Potential Applications" in *Soc. Chem. Ind. (London) Monograph* no. 11, 72, 86 (1961); R. Bentley, "Glucose Oxidase" in *The Enzymes* vol. 7, P. D. Boyer *et al.*, Eds. (Academic Press, New York, 1963) pp 567-586. Review of use as analytical reagent: J. Raba, H. A. Motolla, *Crit. Rev. Anal. Chem.* 25, 1-42 (1995).

Amorphous powder or crystals. Abs max between 270-280, 375-380, and 450-460 nm (aq soln). Freely sol in water giving yellowish-green solns. Most active at pH 5.5-6.0 and 30-35°. Stable between pH 4.5 and 7.0. Stable to pepsin and trypsin. A glucose oxidase unit is defined as that quantity of enzyme which will cause the uptake of 10 mm<sup>3</sup> oxygen per min in a Warburg manometer at 30° in the presence of excess air and excess catalase with a substrate contg 3.3% glucose monohydrate and 0.1M phosphate buffer, pH 5.9 with 0.4% sodium dehydroascorbate: Scott, *J. Agr. Food Chem.* 1, 727 (1953).

USE: Analytical reagent for the selective detection of glucose. Food additive for the removal of glucose during the prep of dried egg products. Antioxidant in food and food wrapper. Stabilizer for ascorbic acid and vitamin B<sub>12</sub>.

4474.  $\alpha$ -Glucose-1-phosphate. [59-56-3]  $\alpha$ -D-Glucopyranose 1-dihydrogenphosphate;  $\alpha$ -glucose-1-phosphoric acid;  $\alpha$ -D-glucopyranose-1-phosphate; Cori ester.  $C_6H_{12}O_6P$ ; mol wt 260.14. C 27.70%, H 5.04%, O 55.35%, P 11.91%. Found widely in both plants and animals. In plants it is the immediate precursor of starch, and in animals of glycogen, being also the first product in the breakdown and utilization of these substances. Isola from muscle and synthesis using trisilver phosphate: Cori *et al.*, *J. Biol. Chem.* 121, 463 (1937); Kral, Cori, *Biochem. Prepn.* 1, 33 (1949). Prep from  $\alpha$ -acetobromoglucose + silver diphenyl phosphate: Posternak, *J. Am. Chem. Soc.* 72, 4824 (1950); by phosphorylation of starch using phosphorylase and orthophosphate: McCready, Hassid, *Biochem. Prepn.* 4, 63 (1955). Structure: Wolfson, Pletcher, *J. Am. Chem. Soc.* 63, 1050 (1941). Configuration: Wolfson *et al.*, *ibid.* 64, 23 (1942); Harmon, *Disc. Abstr.* 24, 4400 (1964); Beevers, Macdonald, *Acta Cryst.* 18, 232 (1965).



Free acid.  $[\alpha]_D^{20} +120^\circ$ .  $pK_1 = 1.11$ ;  $pK_2 = 6.13$ . Stronger acid than  $H_3PO_4$ . Extremely sol in water.

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